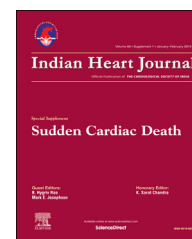


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Review Article

Sudden cardiac death – Historical perspectives

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ABSTRACT

Sudden cardiac death (SCD) is an unexpected death due to cardiac causes that occurs in a short time period (generally within 1 h of symptom onset) in a person with known or unknown cardiac disease. It is believed to be involved in nearly a quarter of human deaths, with ventricular fibrillation being the most common mechanism. It is estimated that more than 7 million lives per year are lost to SCD worldwide. Historical perspectives of SCD are analyzed with a brief description on how the developments in the management of sudden cardiac arrest evolved over time.

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1. Sudden cardiac death (SCD) – historical perspectives

Sudden cardiac death (SCD) describes the unexpected natural death from a cardiac cause within a short time period, generally ≤ 1 h from the onset of symptoms, in a person without any prior condition that would appear fatal.¹ It is estimated that more than 7 million lives per year are lost to SCD worldwide. Nearly a quarter of human deaths are believed to be due to SCDs, with ventricular fibrillation (VF) as the most common mechanism. Interestingly, the concept that SCD in human beings is due to VF was first proposed more than 120 years ago by MacWilliam, well before the electrocardiogram was invented.²

The conceptual evolutions in the understanding of relation between SCD and VF, developmental design of defibrillators and practice of cardiopulmonary resuscitation methods have

undoubtedly improved the survival of patients at higher risk of SCD. The historical perspectives of these three important aspects will be discussed below.

2. Sudden cardiac death and ventricular fibrillation

The sudden collapse and instantaneous death of a person had long intrigued and puzzled medical science and for centuries, no satisfactory explanation was available. The initial description of SCD in the history was made as early as 4th century BC by the first physician and the legendary founder of modern medicine – Hippocrates. Hippocrates stated in his aphorisms that “those who are subject to frequent and severe fainting attacks without obvious cause die suddenly.” This might be the first description of SCD.³ Lyman Brewer suggested that the first recorded account of VF dates as far back as

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1500 BC, and can be found in the Ebers papyrus of ancient Egypt.⁴ It states: “When the heart is diseased, its work is imperfectly performed: the vessels proceeding from the heart become inactive, so that you cannot feel them... if the heart trembles, has little power and sinks, the disease is advanced and death is near.” The next recorded description is from the sixteenth century and is recorded by Vesalius who described the appearance of “worm-like” movements of the heart in animals prior to death. The clinical importance of these observations and descriptions, possibly of VF, were not recognized until John Erichsen in 1842 described VF following the ligation of a coronary artery of a dog.

In 1849, Carl Ludwig and M Hoffa demonstrated that VF could be induced by applying an electric current to the heart of a dog (Fig. 1). It was in the classic work in 1889, “cardiac failure and sudden death” that John A MacWilliam, a British scientist,² first proposed the hypothesis that VF was the mechanism of sudden death in human beings. Until that time, many assumed that sudden death – or “cardiac failure” as it was then commonly called – was due to sudden stoppage of the heart in diastole.⁵ He recognized the role of the autonomic nervous system in modulating both the mechanical and the electrical properties of the heart and was the first to suggest that autonomic nervous system had a role in the genesis of SCD.

MacWilliam also noted that the ventricles contained within them the entire mechanism necessary for the execution of regular coordinated pumping action. Separating the ventricles from the atria physiologically or anatomically by sectioning through the atrioventricular groove showed that the ventricles could function normally; albeit at a slower rate. He demonstrated that in such a sectioned heart too, fibrillation could be induced, demonstrating that extrinsic control was not essential for either ventricular contraction or the induction of fibrillation. His experiments in dogs showed that a fibrillating heart could be brought back to normal rhythm with internal cardiac massage and injectable pilocarpine.^{6,7} These

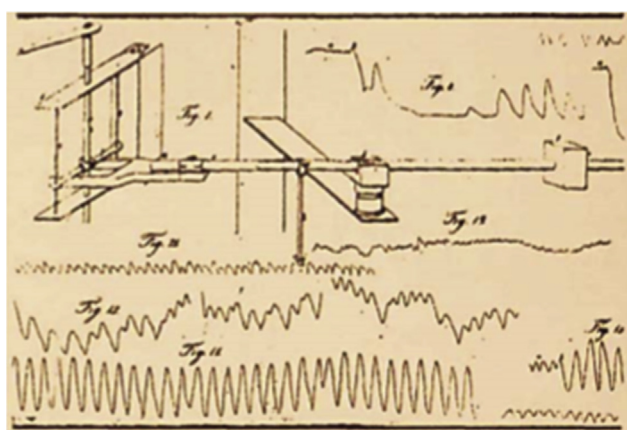


Fig. 1 – The first graphic documentation of ventricular fibrillation. M Hoffa, in Carl Ludwig’s laboratory, while investigating vagal influences on cardiac activity noted the bizarre unregulated actions of the ventricles when exposed to strong faradic or constant currents. The rhythm was noted to persist even after electrical stimulation and to result in no cardiac output. The atria were noted to be free from arrhythmia.

methods were the beginning of a systematic and meaningful approach to successful cardiopulmonary resuscitation.

Ziemssen’s experiments in Munich in 1880 in which a woman’s heart was stimulated with electrical pulses with no apparent harm were the first reports of stimulation of living human heart by electricity.⁸ In 1889, in another paper⁹ MacWilliam commented on the electric treatment of a systole, which he boldly entitled “electrical stimulation of the heart in man”. He wrote that a series of electrical stimulation might be useful in rousing into action a heart arrested by a temporary cause; for example, by inhibitory impulses profoundly depressing the rate and force of its action, or causing it to stand still in diastole. He was careful to point out, however, that application of a strong current would cause VF, especially in a heart compromised by metabolic or structural alterations. The importance of VF in man became clear in the early decades of last century following the development of electrocardiography and its subsequent use in examining cardiac patients.

3. Evolution of defibrillation therapy for SCD

There were two reports on the effects of successful resuscitation in animals and humans using Leyden jar discharges – that of Squires in 1774 and Abilgaard in 1775.¹⁰ The Swiss researchers Jean Luis Prevost and Frédéric Battelli reported in 1899 that low currents provoked VF and that strong discharges terminated this arrhythmia.¹¹

When General Electric, the company cofounded by Thomas Edison, switched from direct current (DC) to alternating current (AC) transmission in the early 1900s, a few linemen died from accidental electrocution. In response, General Electric company funded research at several universities to study what made electric current lethal. Two electrical engineering professors, William Kouwenhoven and Guy Knickerbocker, at Johns Hopkins University, in Baltimore, tested the phenomenon by shocking stray dogs to death. Serendipitously, they noticed that a second AC shock could sometimes bring an electrocuted dog back to life.

In 1933, Albert Hyman and C. Henry Hyman, looking for an alternative to injecting powerful drugs directly into the heart, came up with an invention that used an electrical shock in place of drug injection. This invention was called the *Hyman Otor* where a hollow needle is used to pass an insulated wire between first and second ribs to the right auricle to deliver the electrical shock. However *Hyman Otor* was a failure and was not accepted by the medical community.

3.1. ‘Open chest’ defibrillators

The first use of a defibrillator on a human being was in 1947 by Claude Beck.² He observed that VF could occur even in ‘essentially healthy’ hearts. In an attempt to save such “hearts”, Beck successfully defibrillated a 14-year-old boy being operated on for a congenital chest defect. Open cardiac massage was done for 45 min while waiting for the defibrillator. This first defibrillator used two table spoons as electrodes, a transformer to isolate the patient from the AC wall supply, and a variable resistor to limit the current to a heart-safe value. This early defibrillator by Beck used AC current

and he used the drug procainamide along with to successfully defibrillate the boy to normal sinus rhythm.

Early defibrillators used alternating current from power sockets, transforming the 110–240 V available in the line, to between 300 and 1000 V, to the exposed heart by way of ‘paddle’ type electrodes, where each electrode was a flat or slightly concave metal plate. The technique was often ineffective in reverting VF while morphological studies showed damage to the cells of the heart muscle as well. The nature of the AC machine with a large transformer also made these units very hard to transport, and they tended to be large units on wheels.¹²

3.2. ‘Closed-chest’ defibrillators (external defibrillators)

Until the early 1950s, defibrillation of the heart was possible only when the chest cavity was open during surgery. While the Initial defibrillators used an alternating voltage from a 300 or greater volt through ‘paddle’ type electrodes, the closed-chest defibrillator device developed subsequently used voltages greater than 1000 V, conducted by means of externally applied electrodes through the chest cage to the heart. These defibrillators also used AC as voltage source and were pioneered by Eskin and Klimov. Recipients of closed-chest AC defibrillation tended to suffer unpleasant side effects from the large steady currents, including skin burns and damage to myocardium.

3.3. Direct current as energy source

In 1959, Bernard Lown and Barouh Berkovits⁴ described the “direct current” defibrillation that involved charging of a bank of capacitors to approximately 1000 V with an energy content of 100–200 J, and then delivering the charge through an inductance such as to produce a heavily damped sinusoidal uniphasic wave of finite duration (approximately 5 ms) to the heart by way of paddle electrodes. This direct current was found to be effective in defibrillation and the new technology led to the development of next generation defibrillators. They also developed an understanding of the optimal timing of shock delivery in the cardiac cycle, enabling the application of the device to arrhythmias such as atrial fibrillation, atrial flutter, and supraventricular tachycardias in the technique known as “synchronised cardioversion”. This modification of defibrillator, enabling timed or synchronized defibrillation, was termed cardioverter and the method itself was named cardioversion by Lown.¹³

3.4. Monophasic to biphasic waveforms

The Lown-Berkovits waveform was the standard for defibrillation until the late 1980s in the West. In the former Soviet Union, Gurvich demonstrated the superiority of the biphasic waveform over the monophasic waveform in dogs as early as in 1967.¹⁴ In fact, most of the external defibrillators in the Soviet Union from the early 1970s used biphasic waveforms,¹⁵ which are known in Russia as the Gurvich-Venin waveform. Numerous studies later showed that a biphasic truncated waveform (BTE) had the advantage of being equally effective while requiring the delivery of lower levels of energy to

produce defibrillation.^{16,17} An added benefit was a significant reduction in weight of the machine. The BTE waveform, combined with automatic measurement of transthoracic impedance is the basis for modern defibrillators.

Biphasic defibrillation alternates the direction of the pulses, completing one cycle in approximately 10 ms. Biphasic defibrillation was originally developed and used for implantable cardioverter-defibrillators. When applied to external defibrillators, biphasic defibrillation significantly decreases the energy level necessary for successful defibrillation. Moreover biphasic current also decreases the risk of burns and myocardial damage. A single shock from a monophasic defibrillator could return 60% of cardiac arrest patients to normal sinus rhythm. Numerous studies on biphasic shocks showed that they appear to achieve the same defibrillation success rates as monophasic waveforms but at significantly lower energy levels.¹⁸

3.5. ‘Portable’ external defibrillators

The first so called “portable” defibrillator, made in 1965, weighed 70 kg without batteries and required an ambulance’s starter battery. This was mainly related to the bulkiness of the capacitor that stores the energy needed to shock. Furthermore, excess current produced by these initial devices could damage the heart instead of defibrillating it. This early device had a button that controlled the gas discharge relay; when pressed, it completed a circuit and delivered a strong single pulse from the capacitor through the inductor to the patient. Because dry skin is an insulator, a rescuer had to apply sufficient pressure to overcome its impedance.

These defibrillators required two trained operators: someone to press the paddles against the chest and another to push the button. One of the operators had to first acquire and interpret the electrocardiogram. Then someone had to remove the leads from the electrocardiogram because the shock would otherwise destroy its electronics. The device wasn’t truly portable—each unit weighed between 20 and 40 kg. There was also a possibility of the device being used in the wrong situation like shocking an unresponsive individual who might actually be experiencing a seizure or vasovagal syncope.

Subsequently in the 1980s, flexible adhesive patches coated with a metal chloride gel were developed to transfer current from the wires to the body instead of bulky paddles. These patches reduced the typical contact resistance from about 150 Ω to 75 Ω , that allowed for smaller voltages. The lower voltages meant that defibrillators could be built with higher density electrolytic capacitors and smaller semiconductor switches. Besides, the defibrillation operation required only one person.

Concurrently, switching to biphasic waveform from monophasic waveform reduced the power requirements for defibrillation, in addition to its higher efficacy. Because biphasic waveforms require less power than their precursors, the size of a defibrillator’s components could also shrink. The heavy metal film capacitor was replaced by a lightweight bank of aluminum electrolytic capacitors connected in series, and the heavy iron inductor was eliminated altogether, as it was no longer needed to reduce the peak currents. Taken together,

these changes reduced the weight of the unit from 40 kg to 1.5 kg and made it safer to operate.

3.6. Mobile emergency care units

In 1968, in a landmark study,¹⁹ McNeilly & Pemberton observed that a majority of heart attack deaths occurred soon after the onset of symptoms. Professor Frank Pantridge, Royal Victoria Hospital, Belfast, soon afterwards put forward and implemented the idea of mobile coronary care. As a result, he is known as “the father of emergency medicine.” In 1966, the first mobile defibrillator unit was introduced, under the medical direction of Dr. Pantridge and Dr. Geddes at the Royal Victoria Hospital in Belfast and significant improvements to outcomes of sudden cardiac arrest patients were soon observed. This was the world’s first Mobile coronary care unit (Fig. 2) and thus began the era of management of myocardial infarction outside the hospital. The need for lightweight, battery-operated defibrillators became increasingly obvious and subsequent research focused on reducing the size of these life saving devices.

Technological innovations were evolving in development of devices for automatic defibrillation in public areas and the concept of telephone-controlled defibrillation was suggested in the early 1980s by Buessman et al. This device enabled users to connect patients to electrodes that were monitored by clinical experts at a base station through a telephone line. This enabled the rescuer to use this device remotely, having the benefit of supervision of a trained operator controlling therapy.

3.7. Implantable cardioverter-defibrillator

A further exciting development in defibrillation and treatment of SCD came with the invention of the implantable device, known as an implantable cardioverter-defibrillator (ICD). This was pioneered at Sinai Hospital in Baltimore by a team that included Stephen Heilman and Michel Mirowski, with the help of industrial collaborator Intec systems of Pittsburgh.

Michel Mirowski conceived the idea for an implantable defibrillator while working in Israel. Mirowski trained at Tel Hashomer Hospital in Israel, where his mentor was Harry Heller, who suffered from recurrent VT that was treated with quinidine or procainamide²⁰. It was the SCD of his mentor in 1966 and the recognition that sudden arrhythmic death was a major problem without, at that time, a solution that influenced Mirowski to dedicate his career to design and develop

ICD. In 1968, he accepted a position at Sinai Hospital of Baltimore, as a director of the Coronary Care Unit. Fortunately for this research, the hospital had a division of biomedical engineering and an animal laboratory. At the Sinai, Mirowski joined with Morton Mower, a junior cardiologist with extensive animal research experience, to begin work on an ICD in July 1969. Only a month later, they successfully tested their first crude prototype, made from a broken external defibrillator paddle, on a dog.^{20,21}

The paper describing their work was eventually published after initial rejections, but there remained considerable negativism in the cardiology community toward the concept of the ICD resulting in financial impediment to further research. In 1972 Mirowski began his collaboration with Stephen Heilman, a physician and engineer who had formed a small medical equipment company called Medrad.

The partnership resulted in the production of the first ICD prototype which was successfully implanted in a dog in 1975. This model was further refined and eventually FDA approved it for human use. After Mirowski and Mower enlisted the aid of colleagues at Johns Hopkins Hospital, cardiac surgeon Myron Weisfeldt and electrophysiologist Philip Reed, the first successful human implant of an ICD was performed in February 1980.²² Though the first ICD model was a success, it weighed 225 g, required a thoracotomy for implantation of the electrode patches, and was only capable of defibrillation.

Virtually simultaneously and independently, John Schuder, an Associate Professor of Biophysics and Surgery at the University of Missouri in Columbia, also began work on an implantable defibrillator.²³ Schuder’s work immensely contributed to the evolution of the present day miniature ICD with low-energy, reliable, high-voltage, and biphasic waveform. It was required that a system would detect VF and VT.

Technology evolved further and countless modifications were made to the ICD systems so that the modern ICDs can be implanted without a thoracotomy, possess pacing, cardioversion, and defibrillation capabilities. They are implanted in a way similar to pacemakers and have a pulse generator with shocking capability and shocking coils to deliver energy.

3.8. Subcutaneous ICDs

Multiple randomized trials have established the efficacy of ICDs as a life-saving therapy for individuals at risk of sudden arrhythmic death.²⁴ These conventional ICDs utilize a transvenous lead within the right ventricle for detection as well as defibrillation of arrhythmia. However, many of the complications of ICD therapy are related to the transvenous lead, and are cumulative over time.²⁵ In addition, avoiding implantation of a transvenous lead, including the associated requirement for fluoroscopy, has the potential to simplify the ICD implantation procedure.

Considering these limitations of a conventional ICD system, an entirely subcutaneous ICD (S-ICD) has been developed and now approved for use in many countries. In S-ICD, a bipolar lead is implanted subcutaneously at the left sternal edge in association with a left mid-axillary line subcutaneous generator for far-field detection and defibrillation of ventricular arrhythmias. First implantation of an S-ICD was done in 2009 and the first publication describing clinical use came in



Fig. 2 – The first mobile defibrillator unit introduced in Belfast.

2010.²⁶ The system is only able to deliver very limited post-defibrillation pacing, and therefore is contraindicated in patients with pacing indications, and generally inappropriate for those anticipated to suffer from pace-terminable monomorphic ventricular tachycardia. The need for larger energy for defibrillation and increased incidence of inappropriate shocks remain issues to be sorted out.

4. Evolution of concepts on cardiopulmonary resuscitation

Earliest organized efforts in cardiopulmonary resuscitation had its roots more in drowning than true SCD. In 1740, the Paris Academy of Sciences officially recommended mouth-to-mouth resuscitation for drowning victims and in 1767, the Society for the Recovery of Drowned Persons became the first organized effort to deal with sudden and unexpected death. In 1891, Dr. Friedrich Maass performed the first equivocally documented chest compression in humans.

4.1. Evolution of basic and advanced life support algorithms

James Elam was the first to prove that expired air was sufficient to maintain adequate oxygenation and in 1956, James Elam and Peter Safar invented mouth-to-mouth resuscitation. Subsequently basic life support (BLS) and cardiopulmonary resuscitation (CPR) algorithms were evolved. In 1960, the American Heart Association started a program to acquaint physicians with close-chest cardiac resuscitation and became the forerunner of CPR training for the general public. Leonard Scherlis started the American heart Association's CPR committee, and in 1963, the American Heart Association formally endorsed CPR. Subsequently Advanced Cardiovascular Life Support (ACLS) was developed at the Third National Conference on CPR held in 1979.

Modifications in both BLS and ACLS evolved over the next two decades based on the scientific evidences and further studies. In 2005, the AHA released a statement about Hands-Only CPR, saying that bystanders who witness the sudden collapse of an adult should dial emergency assistance and provide high-quality chest compressions by pushing hard and fast in the middle of the victim's chest. The last update of the guidelines came in the 2010 International Consensus on Emergency Cardiovascular Care (ECC) and CardioPulmonary Resuscitation (CPR) Science with Treatment Recommendations (CoSTR) Conference. This conference conducted at the 50th anniversary of CPR, produced the 2010 American Heart Association Guidelines for CardioPulmonary Resuscitation (CPR) & Emergency Cardiovascular Care (ECC).²⁷

The 2010 AHA Guidelines for CPR and ECC recommend a change in the BLS sequence of steps from A-B-C (Airway, Breathing, Chest compressions) to C-A-B (Chest compressions, Airway, Breathing) for adults, children, and infants (excluding the newly born). A new simplified universal adult BLS algorithm has been created and refinements have been made to recommendations for immediate recognition and activation of the emergency response system based on signs of unresponsiveness, as well as initiation of CPR if the victim

is unresponsive with no breathing or no normal breathing. The existing recommendation of "Look, listen, and feel for breathing" has been removed from the algorithm. Continued emphasis has been placed on high quality CPR (with chest compressions of adequate rate and depth, allowing complete chest recoil after each compression, minimizing interruptions in compressions, and avoiding excessive ventilation).

The links in the new AHA ECC Adult Chain of Survival are as follows:

1. Immediate recognition of cardiac arrest and activation of the emergency response system
2. Early CPR with an emphasis on chest compressions
3. Rapid defibrillation
4. Effective advanced life support
5. Integrated post-cardiac arrest care

Thanks to the advances in the automated external defibrillators, the weak link in the resuscitation chain is now CPR. The classic protocol is for a rescuer to administer manual chest compressions and mouth-to-mouth ventilations until someone brings a defibrillator or an ambulance arrives. This keeps blood oxygenated and moving to forestall brain death. Surprisingly, recent studies have shown that the chest compressions also move some air through the lungs, at least for a few minutes after the onset of cardiac arrest. As a result, mouth-to-mouth breathing is now being dropped from those protocols and the latest AHA guidelines recommend lay rescuers to provide Hands-Only CPR for adults with sudden cardiac arrest.

4.2. Cardiocerebral resuscitation (CCR)

Developed by the University of Arizona Sarver Heart Center Resuscitation Group, cardiocerebral resuscitation (CCR) is a new approach to the resuscitation of patients with cardiac arrest that significantly improves survival with minimal neurological damage.^{28,29} It is composed of 3 components:

- 1) continuous chest compressions (CCCs) for bystander resuscitation.
- 2) a new emergency medical services (EMS) advanced cardiac life support (ACLS) algorithm.
- 3) aggressive post-resuscitation care including therapeutic hypothermia and early catheterization/intervention.

The CCR method advocates continuous chest compressions without mouth-to-mouth ventilations for witnessed cardiac arrest. It advocates prompt defibrillation and early venous access. Endotracheal intubation is delayed, excessive ventilations are avoided, and early administration of epinephrine is advocated.³⁰ However, CCR is not recommended for individuals with respiratory arrest and guidelines recommend CPR for individuals with respiratory arrest.

5. Survival following SCD – current status

Despite advances in technology and awareness; only about 25% of those initially resuscitated survive to leave the hospital. Among those initially resuscitated who do not survive long

term, about one-third die from central nervous system damage, another one-third die from myocardial failure, and the final one-third from a variety of causes including infection and multi-organ failure.³¹ The low incidence of bystander-initiated resuscitation efforts in patients with cardiac arrest is a major public health problem. The initiations of bystander resuscitations, especially when begun within 1 min of the arrest, markedly improve survival.³² It is assumed that removal of mouth-to-mouth respiration from CPR guidelines and hands-only CPR may prompt more people to get involved in cardiac arrest resuscitations and the application of new CCR algorithms hopefully would bring a better survival of these unfortunate victims.

Conflicts of interest

All authors have none to declare.

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